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- The prevalence of disorders detected through newborn screening in Alaska approximates that seen in the US as a whole.
- During 1987-96 in Alaska, Alaska Natives had a high prevalence of congenital adrenal hyperplasia while Asians had a high prevalence of congenital hypothyroidism.
- During 1987-96 females had a higher prevalence of disease for all disorders included in the newborn screen.
- During 1987-96, six infants with significant disease may have been missed because of failure to receive an initial or follow-up newborn screen.

Alaska Newborn Screening Program

Background/History

In the United States, newborn screening began during the early 1960's to detect phenylketonuria (PKU), a major cause of severe mental retardation before the discovery of treatment by a phenylalanine restricted diet. The Alaska Legislature passed a statute during 1967 requiring physicians and nurses to test all newborns for PKU, with wording to expand testing "to other heritable diseases which lead to mental retardation and physical handicaps" as tests became available. Diseases were selected based on their inability to be detected clinically at birth, their severity, their population prevalence, and the availability of a diagnostic test and effective intervention.

Currently, all states test for PKU and congenital hypothyroidism (Office of Technology Assesment, 1988; American Academy of Pediatrics, 1996). Individual states have added other diseases based on the specific needs of the states' population. For Alaska , quality assurance, economy and an expanded list of diseases were reasons to join Oregon's Regional Newborn Screening Program from 1975-81 and to return to this program during 1987.

In addition to PKU, congenital hypothyroidism, galactosemia, maple syrup urine disease, and biotinidase deficiency, Alaska includes congenital adrenal hyperplasia as part of the newborn screening panel because of the known increased gene frequency of 21-hydroxylase deficiency among Yupik Eskimos (Hirschfield & Fleshman, 1969; Pang et al, 1988). While other states in the Pacific Northwest Region test for hemoglobinopathies, evidence suggests this would not be cost-effective in Alaska (Gessner et al, 1996). Health care providers may request hemoglobin testing on the newborn screen for an additional fee of $3.00.

By the 1990's there were growing concerns regarding mail delays of specimens and the impact of early hospital discharge on testing. The Alaska Newborn Screening Program assumed additional responsibilities to ensure that all infants received screening, including monitoring hospital discharge screening, matching names of newborns provided by hospitals to names on screening tests, and following positive test results until confirmation and treatment.

Methodology

Nationally, no federal regulations govern screening and there is no single universally accepted laboratory procedure for testing newborn screening samples. Alaska regulations require that all specimens be collected as blood spots on a standard filter paper ("Guthrie card") and mailed to a central laboratory. The initial specimen should be collected from the infant as close to hospital discharge as possible and no later than seven days of age. The Alaska Newborn Screening Program charges $24.00 per infant, which includes all screening and confirmatory tests if confirmation is done through the Newborn Screening Program.

Disorders Detected

From July 1987 through August 1996, the Alaska Newborn Screening Program identified 76 affected infants (Table 1). During this same period, an estimated 110,000 births occurred (birth figures for 1995-96 are estimated). Congenital hypothyroidism occurred more frequently than any other disorder and its prevalence in Alaska was similar to other state and national figures (Newborn Screening Committee, 1993)

Each state newborn screening program selects diseases that can be expected to occur with a certain frequency given the genetic background of the state's population. For example, nationally PKU occurs more commonly among persons of Northern European descent, congenital adrenal hyperplasia occurs more commonly among Yupik Eskimos, and congenital hypothyroidism occurs among all races. Data from Alaska demonstrates that disorders occur among each ethnic group. Among all disorders detected during 1987-96, 45% occurred among whites, 25% among Alaska Natives, 9% among Asians, 4% among blacks, and 16% among others or persons of unknown race. The distribution of disorders varied by race (Table 2). Persons included in the category "Other race", primarily Asians, have a high prevalence of congenital hypothyroidism for unknown reasons.

The prevalence of all disorders varied by gender between females and males. For each disorder, more females than males were detected (Figure 1). Neonatal hypothyroidism affects females more often than males 2:1 worldwide, but the gender bias seen in Alaska for other disorders is unexpected since these are inherited as autosomal recessive disorders.

Table 1. Disorders detected by newborn screening; Alaska, 1987-96

Disorder	Frequency	Alaska live birth prevalence	US live birth prevalence*
Congenital hypothyroidism**	41	1:2700	1:3600-5000
Congenital adrenal hyperplasia	19	1:5700	1:12,000***
Phenylketonuria	12	1:9000	1:10,000-25,000
Galactosemia	3	1:36,600	1:60,000-80,000
Biotinidase deficiency	1	1:110,000	1:72,000-126,000
Maple Syrup Disease	0	0	1:250,000-400,000
Total	76	1:1447	

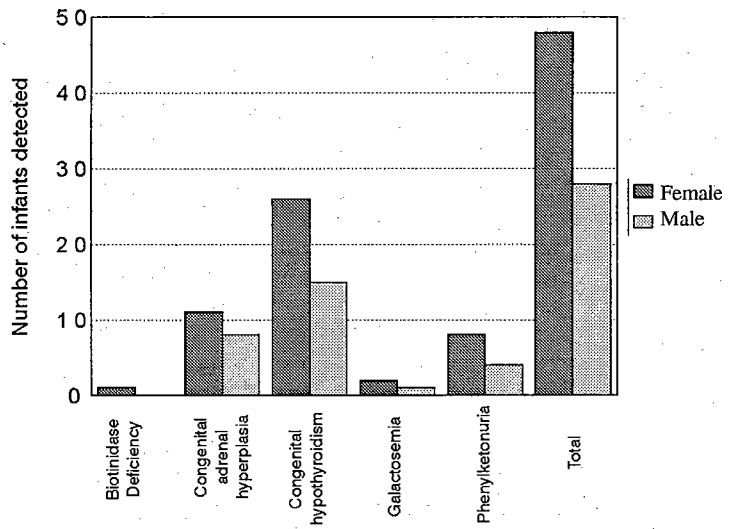
*American Academy of Pediatrics, 1996
**Congenital hypothyroidism and hypopituitary hypothyroidism
***Prevalence among Yupik Eskimos equaled 1:680

Table 2. The overall incidence of disorders detected by newborn screening, by race; Alaska, 1987-96

Race	Phenylketonuria	Congenital adrenal hyperplasia	Congenital hypothyroidism	All Disorders
White	1:8400	1:18,800	1:3800	1:2200
Native	1:25,200	1:1900	1:5000	1:1300
Black	1:5000	0	1:5000	1:1700
Other*	0	0	1:800	1:700

*Vital statistic data did not include Asian populations separately until 1994.

Figure 1. The number of disorders detected by newborn screening, by gender, and type of disorder; Alaska, 1987-96.



Components of Newborn Screening Programs

Although the individual diseases occur infrequently, states have adopted newborn screening programs because early identification and treatment greatly improves prognosis, because of the severity of the effects of untreated disorders, and because of the burden children with untreated disorders place on their family and society. National goals include detection of all tested conditions within the first week of life, confirmation of the diagnosis, and initiation of treatment by 21 days of age.

Elements of Effective Newborn Screening

I. Universal Screening

During 1995, 11,128 specimens were collected from an estimated 10,600 infants. Hospitals and midwives reported the names of 9667 (95.1% of births) newborns to the Alaska Newborn Screening Program. The Alaska Newborn Screening Program matched these names to the names on specimens received at the newborn screening laboratory. Hospitals were alerted each week regarding infants who had not been tested or whose specimens had not been received by the laboratory.

Table 3. Median age at initiation of treatment for disorders detected during newborn screening; Alaska, 1987-96.

Disorder	Median age, in days at initiation of treatment	(range)
Phenylketonuria	13	(2-90)
Congenital Hypothyroidism	18	(1-68)
Congenital Adrenal Hyperplasia	5	(1-88)
Galactosemia	7	(5-22)
Maple Syrup Urine Disease		
Biotinidase Deficiency	31	(31)

Overall, 4.9% of infants born in Alaska were not reported to the Alaska Newborn Screening Program. Among these infants, some did not have a newborn screening card collected, most commonly because of very early hospital discharge and hospital transfer. Two percent of infants were not tested because of parent refusal; refusal rates exceeded 20% of deliveries at three small hospitals. Some of the infants who did not receive hospital testing may have received testing by their primary providers after discharge.

II. Collection of Appropriate Specimen at Proper Time

No single optimum time exists for screening all six disorders. To clarify timing guidelines, Alaska regulations require testing before hospital discharge regardless of age. Infants born out of hospital should receive testing during the first week of life. For all infants, if their first test occurs before 48 hours of age, they should have a second specimen collected before 21 days of life. If the first test occurs between 48 hours and 7 days, a second test is recommended but not required. National statistics indicate that 95% of affected infants have abnormal test results on the first test regardless of age or feeding schedule.

Infant's age at collection: In Alaska during 1995, 69% of initial specimens were collected at or before 48 hours of age, 88% by 5 days of age, and 91% by 7 days. Of the remainder, 4% were collected beyond 7 days of age and 5% did not have either a birth or collection date recorded. Some infants may have had testing beyond 7 days of age because of repeated initial tests (due to name changes, lost cards, or unavailable test results).

Follow-up testing: All screening tests, except those which detect amino acid disorders, measure levels of specific enzymes or detect protein markers for hemoglobin varients. Consequently, testing soon after birth may provide accurate results and allows rapid initiation of therapy. Despite this some infants with significant disorders will have a negative initial test but a positive follow-up test.

The percentage of infants tested at or before 48 hours of age continues to increase each year in Alaska and nationally. Because of the early first test, these infants will require two tests. During 1995, 70% of infants had two or more tests. Of the 76 infants with abnormalities detected through screening during 1987-96, eight (11%) were detected on the second test, including five with congenital hypothyroidism and three with congenital adrenal hyperplasia.

Missing data: Congenital hypothyroidism and congenital adrenal hyperplasia are the most common disorders detected. Because normal values for both of these disorders are age and weight adjusted, when this data is missing from the specimen card interpretation of results becomes difficult. During 1995, 6.4% of samples did not have birthdate, collection date, weight, or sex.

Improper Specimen: One percent of specimens submitted to the laboratory during 1995 required repeat testing because of insufficient blood, improper collection, or contamination.

Transit delays: Health care providers should mail specimens within 24 hours of collection. Mail delays can occur due to in-house mail systems, inefficient courier services, and US postal delays during holiday seasons. For 1995 specimens, the average transit time from hospital to laboratory was 5 days, with a range from 3-9 days.

III. Initiation Of Treatment

The speed with which a diagnosis occurs and treatment initiated provides one measure of the efficiency and effectiveness of a newborn screening program. For most disorders, infants should have treatment initiated before 21 days of life. During 1987-96, the age at which treatment began ranged from 1 to 90 days (Table 3). While 75% of infants started treatment before 21 days of age, 19 did not have treatment initiated until 21 days or later. Fortunately, significant improvement has occurred during the last five years.

Consequences of Failures to Properly Screen Newborns

The shortcomings described above may have serious consequences for infants.

- Approximately 4% of infants did not receive an initial test. Based on the overall incidence of disorders of 1:1450 infants and 110,000 births during a ten year period, this suggests that three infants had disorders which were not detected on newborn screen.
- During 1995, only 70% of infants received a second screening test yet the second screen detected 11% of disorders during 1987-96. Assuming that the rate of second screening was not better during the years preceding 1995, this suggests that three additional infants during 1987-96 did not have a disorder detected because they failed to receive a second test.
- Nineteen infants did not have treatment initiated in a timely fashion which may lead to the infant having permanent impairment.

Conclusions

Nationally, the **Year 2000 & MCH Objectives** relating to newborn screening are to increase to at least 95% the

proportion of newborns screened by state-sponsored programs for genetic disorders (and other disabling conditions) and to increase to 90% the proportion of newborns testing positive for disease who receive appropriate treatment. During 1995, the Alaska Newborn Screening Program achieved these objectives. Despite this achievement, as many as six infants may have had a disorder which was not detected and 19 had a disorder detected but had treatment initiated after the recommended time.

Several steps have been taken to address these problems. The Alaska Administrative Code has been revised to clarify practitioner responsibilities and procedural guidelines. The State of Alaska has taken an increasingly active role in monitoring the program for untested infants and following up positive test results. Recent federal legislation requiring insurance companies to provide payment for hospital stays of up to 48 hours for newborns may decrease the number of infants discharged before screening occurs. In addition to these steps, we recommend the following:

1. All infants should receive testing before hospital discharge, and information on specimen cards should be filled out completely. Infants born out of hospital should receive testing within the first week of life. Specimens should be mailed within 24 hours.

2. Health care providers who see infants after the newborn period should document when the infant received the initial newborn screen and ensure that the required or recommended second test is obtained.

3. Health care providers should work to educate parents who refuse newborn screening for their infant about the potential benefits and minimal risks associated with testing.

The Alaska Newborn Screening Program seeks to identify affected infants born in Alaska and to initiate treatment before damage occurs. To achieve this goal, an ongoing coordinated effort must exist between local practitioners, the Oregon laboratory, and the State of Alaska. To assist with this effort, a newborn screening manual-describing disorders, standards, and common problems in screening practices and other technical assistance is available through the Alaska Division of Public Health, Section of Maternal, Child, and Family Health, Newborn Screening Coordinator *(phone number 907-269-3430).*

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